IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of:	Art Unit: 2819
S. KADOTA	Examiner: M. FLOOD
Appl. No.: 10/825,585	Atty. Docket: 0804.001.0002
Filed: April 16, 2004	Confirmation No.: 8180
For: **Agents for Treating Osteoporosis and Inhibiting Osteoclast Formation**	Customer No.: 43446

DECLARATION UNDER 37 C.F.R.§1.132

Mail Stop Amendment
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

1. My name is Chia-Chin Sheu and I am employed by the Assignee of the above-identified patent application. I have been employed by the Assignee in the position of President of Simpson Biotech Co., Ltd. since Oct 1998.

2. I have a background in Bio-chemistry & Analytical Chemistry / Master of Sci.

3. I understand that the claims of the above-identified patent application have been rejected over Tadetomo et al. and Yoshii.

4. I performed the following experiments, which depict differences between a water extract of *Cordyceps sinensis* obtained using an organic solvent in the process and a water extract without using an organic solvent in the process.

Method:

A). Sample Preparation:

a). **Deionized water extract**
Sample Name CS (H_2O)

1). Precisely weighed 0.500 (g) of *Cordyceps sinensis* mycelia in 20 ml of sample vial, added 10 ml of deionized water extracted 30 minutes by ultrasonic water bath.
2). After centrifuge, took top liquid layer for HPLC analysis.

b). **Organic solvents then deionized water extract**
Sample Name CS (ether, MeOH, H2O)

1). Precisely weighed 10.000 (g) of *Cordyceps sinensis* mycelia in extraction apparatus with 300 ml of ether, then extracted 2 hours.
2). After centrifuging the residue added 300 ml methyl alcohol in extraction apparatus with 300 ml of ether, then extracted 2 hours.
3). After centrifuging the residue added 300 ml deionized water in extraction apparatus with 300 ml of ether, then extracted 2 hours.
4). After centrifuging, the top liquid layer was taken for freeze-dryer, then precisely weighed equal amount of powder dissolved in deionized water for HPLC analysis.

B). Analyzed by Waters™ 2690 Separations Module system:

1). Waters GPC column: Ultrahydrogel & HSPgel AQ serial connection
2). Mobile phase: deionized water (LC grade).
3). Flow rate: 0.3 ml/min.
4). Temperature: 30°C.
5). Wavelength: 254 nm.
6). Injection volumn:10 μl.
7). Detector: serial connection with Refractive Index 2414 、Photodiode Array 996 and Conductivity 431 Detector.

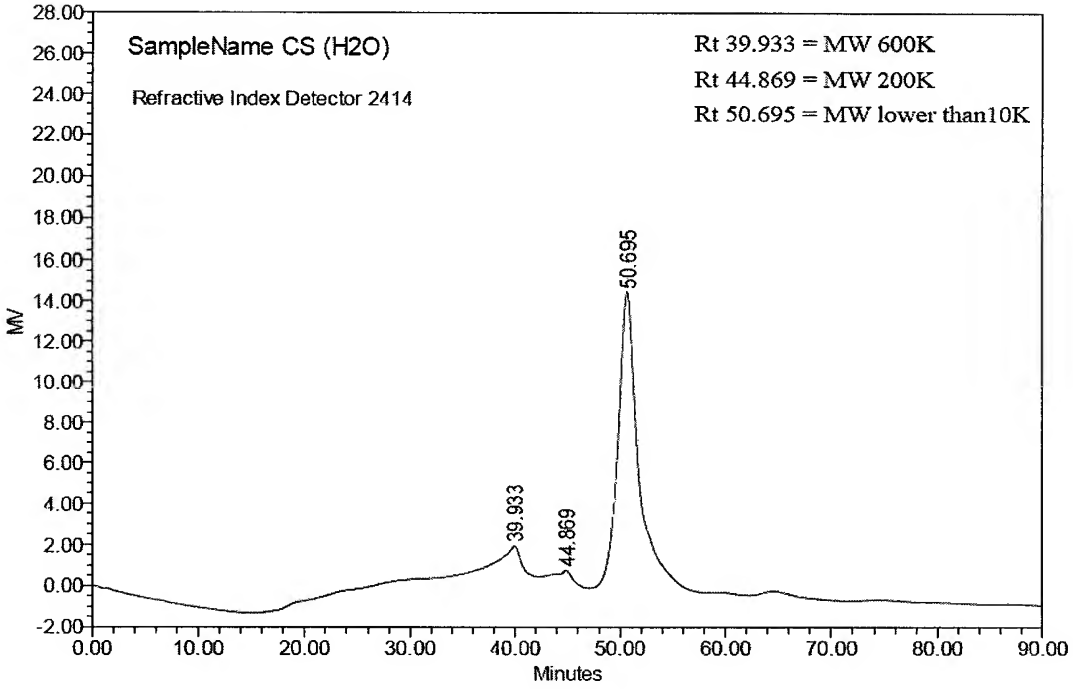
Results:

After extraction by the above procedures, Simpson Biotech *Cordyceps sinensis* mycelia chromatograms by serial connection three detectors reveal several clues. Details of chromatograms are shown in following pages. According to these results, the following are suggested:

A). Refractive Index Detector 2414 detected two chromatograms in Fig.1. These two chromatograms are different in extraction procedures and retention time of peaks. In the top diagram, from CS (H2O) deionized water extract, the substance obtains Retention Time (Rt) of 50.7 minutes, which corresponds to small size of molecule, MW lower than 10K. In the bottom diagram, from CS (ether, MeOH, H2O) organic solvents then deionized water extract, the substance obtains aRetention Time (Rt) of 20.28 minutes, which corresponds to huge size of molecule, MW more than 2000K. Therefore, these two chromatograms suggest that the substance extracts are different particularly in molecule size.

B). Photodiode Array Detector 996 detected two chromatograms in Fig.2, and Conductivity Detector 431 detected two chromatograms in Fig.3. Diagrams in both Fig.2 and Fig.3 also suggest that the substances extracted are different, particularly in molecule size. Photodiode array detector could analyze proteins, and conductivity detector detects substances with charge.

Fig. 1 Chromatograms detected from Refractive Index Detector 2414



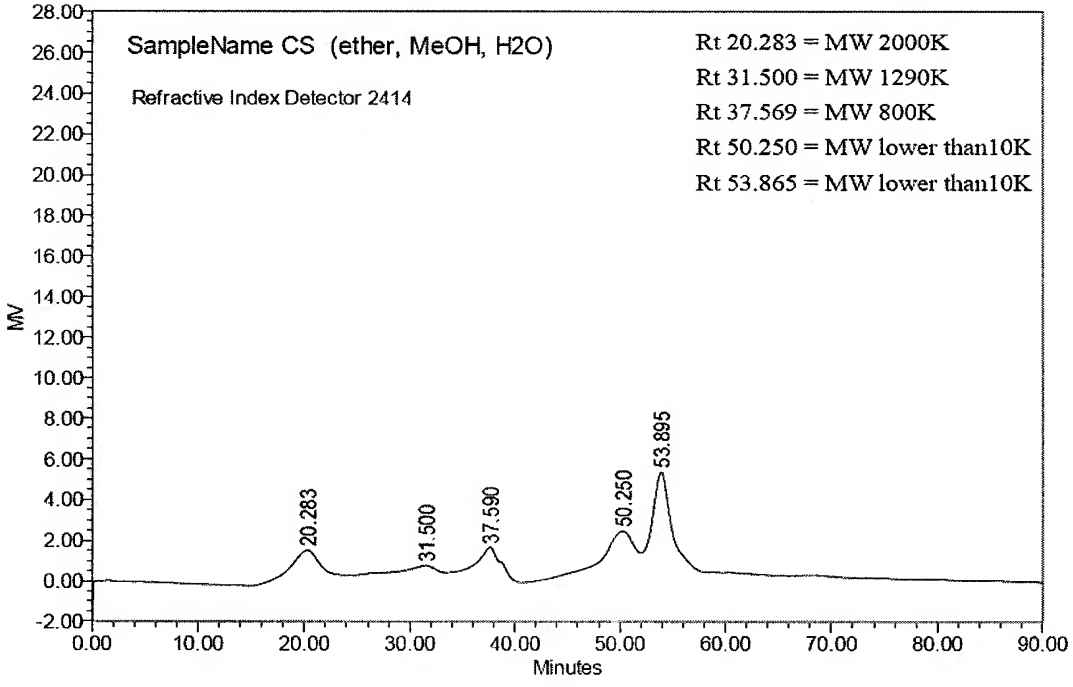
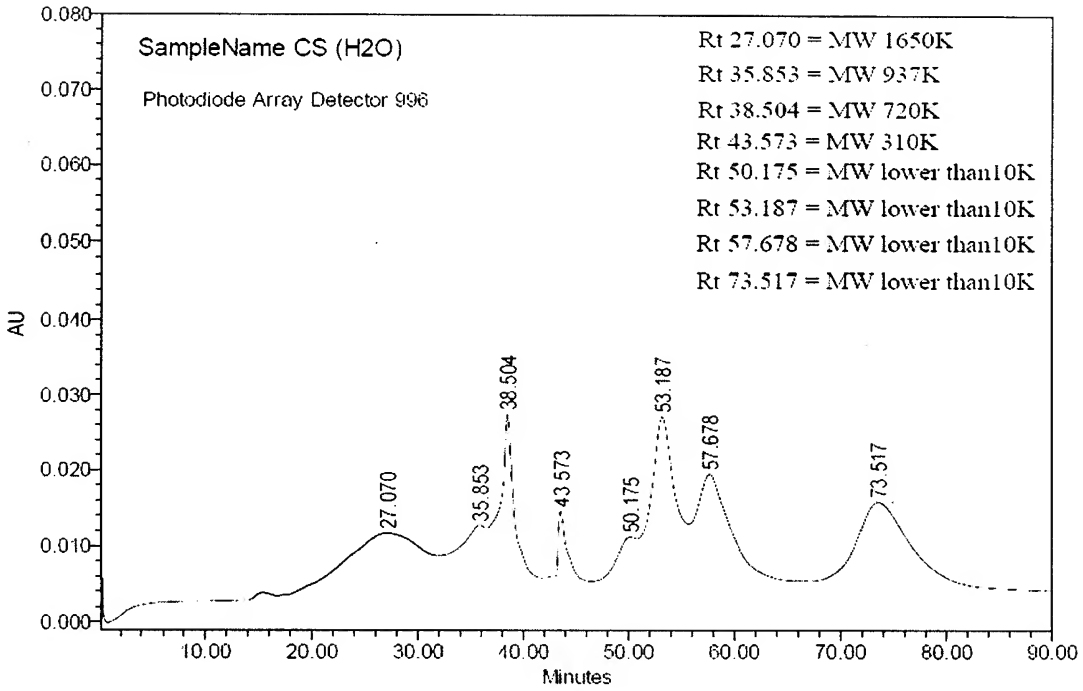


Fig. 2 Chromatograms detected from Photodiode Array Detector 996



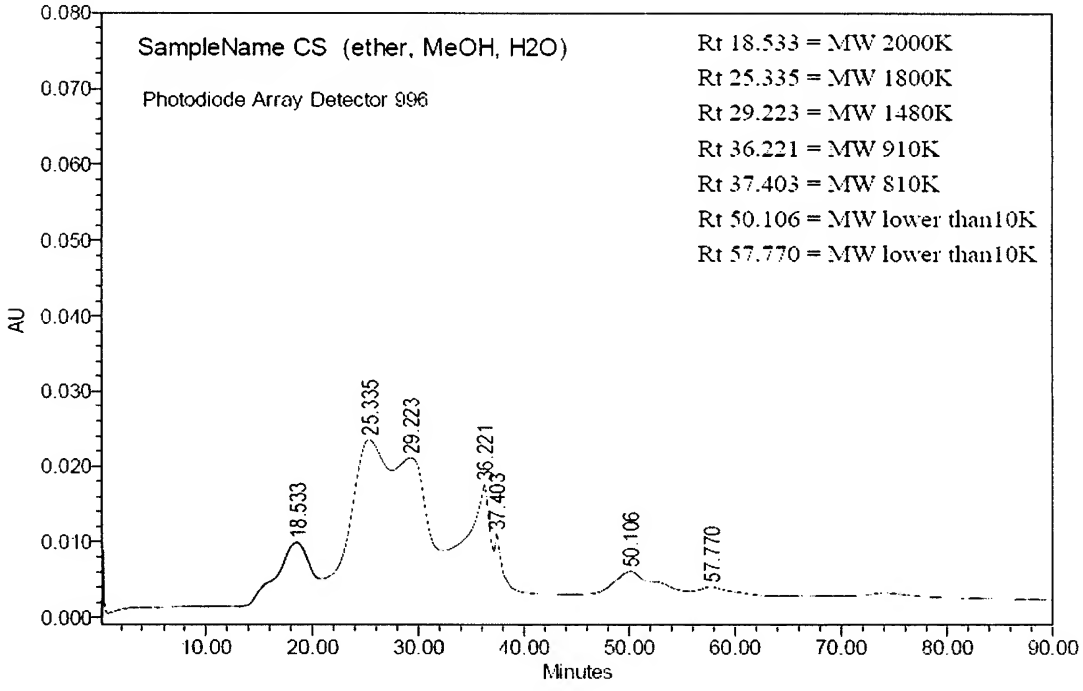
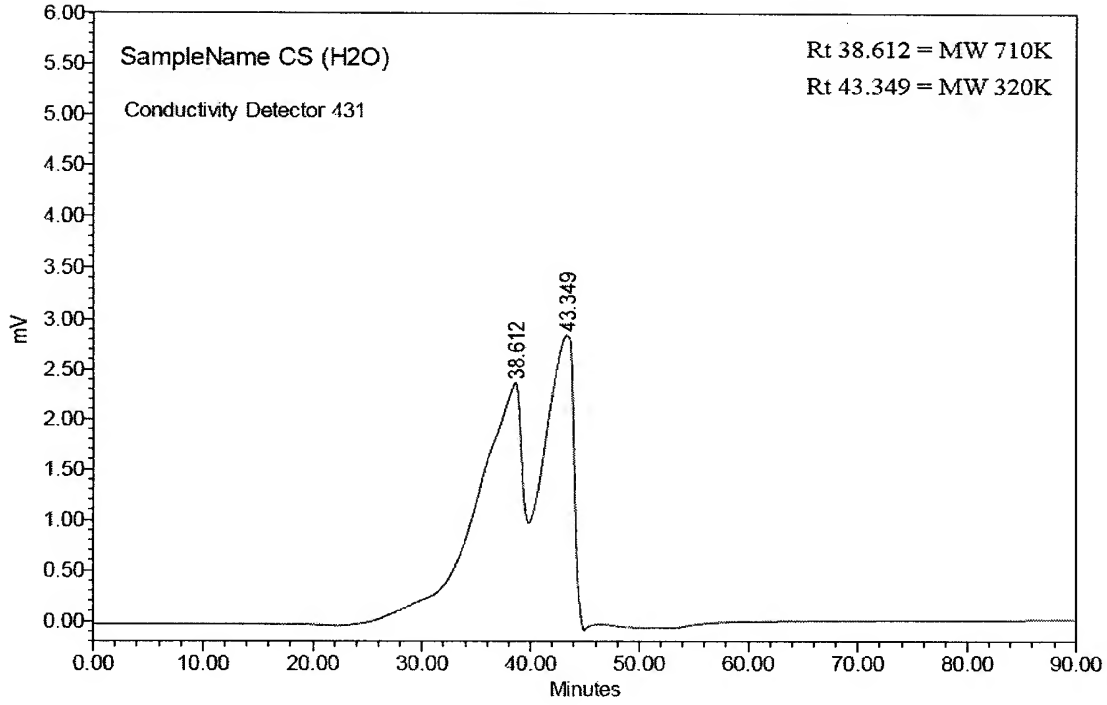
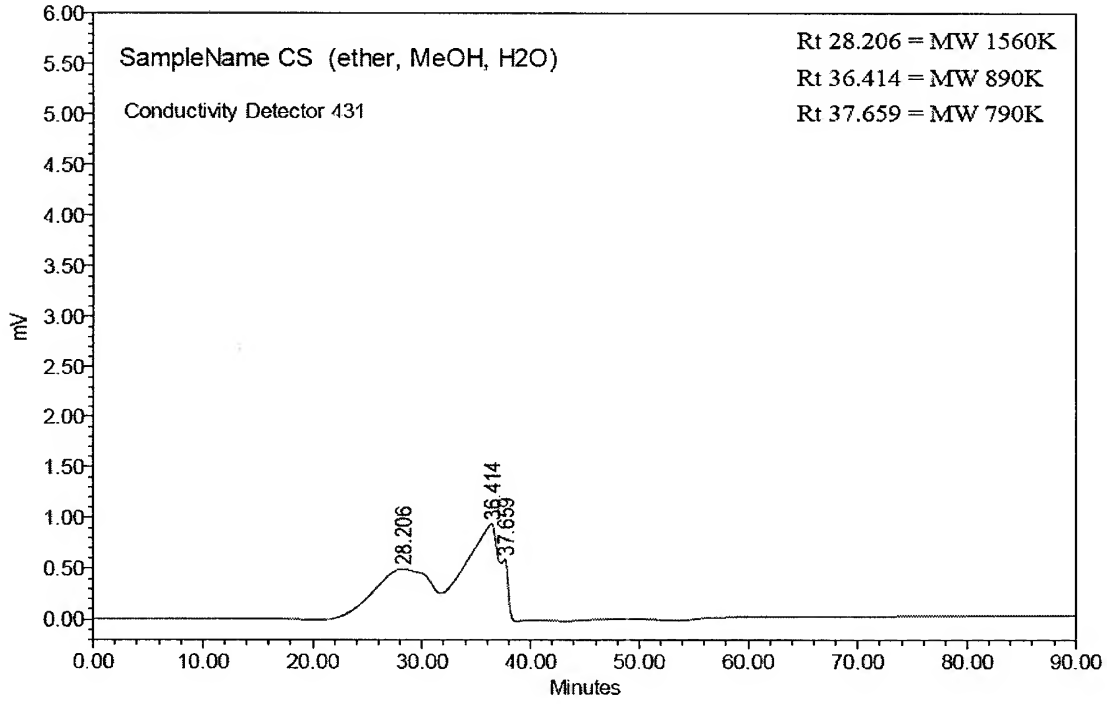


Fig. 3 Chromatograms detected from Conductivity Detector 431





Conclusion:

These chromatograms from Simpson Biotech *Cordyceps sinensis* mycelia, depict the products of different extraction procedures, deionized water extracts well as organic solvents then deionized water extract. Therefore, all of chromatograms suggest that these two extracts are different particularly in molecule size.

5. I declare under penalty of perjury that I have performed the above-identified experiment and that the information contained herein is **true and correct**.

Executed at Taipei, Taiwan, R.O.C. on March 12, 2007.